REMARKS

The Examiner rejected claims 22 and 23, while withdrawing claims 1-21 and 24-33 from consideration. Claims 24, 25, and 28-37 are canceled herein without prejudice, and new claims 38-43 are added. In view of the amendments presented herein and the remarks below traversing the restriction to claims 22 and 23, Applicants respectfully submit that claims 11-17, 21-23, 26, 27, and 38-43 are pending, while claims 1-10 and 18-20 stand withdrawn.

Claims 11, 14, and 21 are amended herein to recite a nucleic acid sequence encoding a polypeptide comprising an amino acid sequence having at least 70% identity with the amino acid sequence set forth in SEQ ID NO:4 or SEQ ID NO:30, or the complement thereof. Claims 12, 13, 16, 17, and 27 are amended herein for consistency with amended claims 11, 14, and 21. Support for these amendments can be found, for example, in original claims 1, 4, and 5, and in Table 2 at page 25 of Applicants' specification, which discloses that the human AMPK gamma subunit is at least 70% identical to the pig AMPK gamma subunit. Thus, SEQ ID NO:4 and SEQ ID NO:30 fall within the scope of claim 1 (i.e., have amino acid sequences that are at least 70% identical to the sequence of SEQ ID NO:2).

In addition, claim 22 is amended herein to remove non-elected subject matter, and claim 23 is amended to recite a method that includes contacting a nucleic acid sample with an oligonucleotide probe, wherein the probe is complementary to a segment of the nucleic acid sequence that includes a mutation, and wherein the contacting is under conditions of specific hybridization between the probe and the mutant sequence to be detected, and detecting the hybridization complex. Support for this amendment can be found in Applicants' specification at, for example, page 15, lines 13-19, which disclose allele specific PCR and allele specific oligonucleotide screening methods.

Further, new claims 38-43 depend from claims 11, 14, and 21, and recite amino acid sequences having at least 80% or at least 90% sequence identity with the sequence set forth in SEQ ID NO:4 or SEQ ID NO:30. Support for these claims can be found in Applicants' specification at, for example, page 4, lines 18-27, which disclose that a polypeptide can have an amino acid sequence with at least 80% or at least 90% identity to SEQ ID NO:2, and in Table 2

at page 25, which discloses that pig and human AMPK gamma subunits have at least 90% sequence identity. Thus, no new matter has been added.

In light of these amendments and the following remarks, Applicants respectfully request reconsideration and allowance of claims 11-17, 21-23, 26, 27, and 38-43.

Restriction/Election

Applicants confirm election of claims 11-17, 21-23, and 26-28 as they relate to isolated DNA sequences encoding a human AMPK subunit and a splice variant thereof (SEQ ID NOS:4 and 30). Applicants further note, however, that this election is classified as Group II(b) rather than Group II(a).

The Examiner stated that there is no reason to withdraw the restriction between Groups II(a) and II(b), because "[t]he fact that porcine and human AMPKs are not structurally identical (i.e., 100% identical) suggest that in contrast to applicant's view the function of said products must be significantly different in nature, rendering them subject to lack of unity as stated previously." Applicants disagree. To reiterate and expand on Applicants' previous comments in the Response filed on December 16, 2005, the human AMPK amino acid sequence set forth in SEQ ID NO:4 is 97% identical to the pig AMPK sequences set forth in SEQ ID NOS:2, 28, and 32. The human AMPK sequence set forth in SEQ ID NO:30 is 97% identical to the pig AMPK sequence set forth in SEQ ID NO:2, and 86% identical to the pig sequences set forth in SEQ ID NOS:28 and 32. Thus, there is significant identity between the pig and human AMPK proteins. Applicants respectfully note that 100% amino acid sequence identity is not a requirement for two proteins (e.g., having the amino acid sequences set forth in SEQ ID NOS:4 and 2 or SEQ ID NOS:30 and 28) to have the same or similar functions.

The Examiner also stated that Group II [(b)] should have been directed merely to claims 22 and 23, as these are the only claims directed to SEQ ID NOS:4 and 30. Moreover, the Examiner appears only to have examined claims 22 and 23. Applicants traverse this further restriction. Previous claim 11, for example, recited a nucleic acid sequence encoding a polypeptide of claim 1, and thus was drawn to a nucleic acid encoding a gamma subunit of a vertebrate AMPK, wherein the gamma subunit is a polypeptide comprising at least a sequence

having at least 70% identity with the sequence of SEQ ID NO:2. As discussed above, SEQ ID NOS:4 and 30 are more than 70% identical to SEQ ID NO:2, and thus are encompassed within the scope of the previous claim. To further prosecution, however, claims 11, 14, and 21 are amended herein to recite a nucleic acid sequence encoding a polypeptide comprising an amino acid sequence having at least 70% identity with the amino acid sequence set forth in SEQ ID NO:4 or SEQ ID NO:30.

In light of the above, Applicants respectfully request rejoinder and examination of claims 11-17, 21, 26, and 27.

Claim objections

The Examiner objected to claims 22 and 23 because they depend from claim 21, which the Examiner has withdrawn as non-elected. In light of Applicants' traverse of the further restriction and the amendment to claim 21, Applicants respectfully request withdrawal of the objection to claims 22 and 23.

Rejections under 35 U.S.C. § 112

The Examiner rejected claim 23 under 35 U.S.C. § 112, second paragraph, as allegedly being indefinite. Specifically, the Examiner asserted that the term "specific hybridization" is unclear because stringent conditions are not explicitly defined in terms of salt and temperature.

Applicants respectfully disagree. Present claim 23 recites that the presence of the nucleic acid sequence encoding the mutant polypeptide is checked by contacting the nucleic acid sample with an oligonucleotide probe, wherein the probe is complementary to a segment of the nucleic acid sequence that includes the mutation, and wherein the contacting is under conditions of specific hybridization between the probe and the mutant sequence to be detected. A person having ordinary skill in the art, reading the specification at the time Applicants filed, would have understood the meaning of the term "specific hybridization." See, for example, page 15, lines 13-19, which disclose that methods allowing for specific hybridization of a probe only with a perfectly matching complementary sequence are known in the art, including procedures such as

allele specific PCR and allele specific oligonucleotide screening. In fact, two references teaching such methods are cited in this section of the specification. Thus, claim 23 is definite.

In light of the above, Applicants respectfully request withdrawal of this rejection of claim 23 under 35 U.S.C. § 112, second paragraph.

The Examiner also rejected claims 22 and 23 under 35 U.S.C. § 112, second paragraph, as allegedly being indefinite. In particular, the Examiner asserted that the term "functionally altered allele" is unclear because it is indefinite how, for example, SEQ ID NO:4 (305 amino acids) and SEQ ID NO:30 (464 amino acids) can both have a mutation at position 41 (i.e., the R41Q variant).

Applicants respectfully disagree. The meaning of the term "R41Q," as well as the term "V40I," is clear. This is particularly true given that these terms are defined at page 8, lines 3-22 of Applicants' specification. In particular, this section of the specification discloses that the residue numbers refer to the amino acid sequences set forth in SEQ ID NOS:2 and 4. Moreover, the arrow in Figure 3 indicates the location of the R41Q mutation at position 201 of SEQ ID NO:30. *See*, e.g., Applicants' specification at page 24, lines 25-26, page 25, lines 25-28, and page 27, lines 29-31. Thus, a person of ordinary skill in the art would have understood the location of the exemplary mutations, and the claims are clear and definite.

In light of the above, Applicants respectfully request withdrawal of this rejection of claims 22 and 23 under 35 U.S.C. § 112, second paragraph.

The Examiner rejected claims 22 and 23 under 35 U.S.C. § 112, first paragraph, for alleged lack of enablement. The Examiner asserted that the specification does not reasonably provide enablement for a method of detecting a metabolic disorder correlated with an altered glycogen accumulation in muscular cells of a vertebrate that results from expression of a functionally altered allele of SEQ ID NO:30, and that undue experimentation would have been required to practice the claimed methods. In particular, the Examiner stated that while the specification discloses regions in SEQ ID NO:4 containing mutations responsible for functional alterations, no information about equivalent regions in SEQ ID NO:30 is provided. In addition,

the Examiner stated that Figure 3 is confusing because it displays the CBS1 domain as starting at residue 72 of SEQ ID NO:4 (HumG3), which is past residues 30-50.

Applicants respectfully disagree. The presently claimed methods are fully enabled. Applicants note that the HumG3 sequence shown in Figure 3 is SEQ ID NO:30, which is the amino acid sequence deduced from the complete cDNA sequence. *See*, e.g., Applicants' specification at page 25, lines 17-28. Further, the arrow shown in Figure 3 indicates the location of the RN (R41Q) mutation. *See*, e.g., page 24, lines 8-26 and page 27, lines 29-31. A person having ordinary skill in the art at the time Applicants filed would readily have been able to align SEQ ID NOS:4 and 30 to ascertain that SEQ ID NO:30 has 159 additional amino acids at its N-terminus as compared to SEQ ID NO:4, and thus the region between amino acids 30-50 of SEQ ID NO:4 corresponds to amino acids 189-209 of SEQ ID NO:30. Given the teachings of Applicants' specification with regard to methods for detecting a mutant allele within this region (*see*, e.g., Example 2 beginning at page 30, line 35), no undue experimentation would have been required for a person of ordinary skill in the art to carry out the method recited in present claims 22 and 23.

In light of the above, Applicants respectfully request withdrawal of the rejection of claims 22 and 23 under 35 U.S.C. § 112, first paragraph.

Allowable subject matter

Applicants acknowledge the Examiner's comments regarding the sequences set forth in SEQ ID NOS: 4 and 30.

CONCLUSION

Applicants submit that claims 11-17, 21-23, 26, 27, and 38-43 are in condition for allowance, which action is respectfully requested. The Examiner is invited to telephone the undersigned agent if such would further prosecution.

Please charge $225 for the Petition for Extension of Time fee, and apply any other charges or credits, to deposit account 06-1050.

Respectfully submitted,

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